REMARKS

Claims 28, 30-43, 45-56, 59, 61-67, and 70-82 are pending in the application.

Applicant respectfully submits that present claims are in condition for allowance or in better form for appeal.

Claims 46-48, 52-56, 59, and 61-66 stand rejected under 35 U.S.C. §102(b) as anticipated by "Enhancement of Molecular Fluorescence Near the Surface of Colloidal Metal Films", by Sokolov et al., Anal. Chem. 1998, 70, 3898-3905, hereinafter, Sokolov.

Claims 28, 30-43, 45, 67, and 70-82 stand rejected under 35 U.S.C. §103(a) as unpatentable over "Surface-Enhanced Raman Spectroscopy Using Metallic Nanostructures, Trends in Analytical Chemistry", by Vo-Dinh, Vol. 17, No. 8-9, 1998, pages 557-582, hereinafter, Vo-Dinh (1998), in view of "Biosensors and Biochips: Advances in Biological and Medical Diagnostics" by Vo-Dinh et al., Fresenius J Anal Chem, (2000) 366: 540-551, hereinafter, Vo-Dinh (2000).

Applicant respectfully traverses the rejections based on the following discussion.

I. The Prior Art Rejections

A. The 35 U.S.C. 102(b) Rejection over Sokolov

1. The Sokolov Disclosure

Sokolov discloses that fluorescence enhancement was studied on silver colloidal metal films (CMFs) using two system: (1)Langmuir-Blodgett monolayers of fluorescein-labeled phospholipids separated from the surface of the films by space layers of octadecanoic acid and (2) biotin-fluorescein conjugates captured by avidin molecules adsorbed on top of a multilayer structure formed by alternating layers of bovine serum albumin-biotin conjugate (BSA-biotin) and avidin. The dependence of fluorescence intensity on the number of lipid or protein spacer layers deposited on the surface of the CMF was investigated. (Abstract, lines 1-11).

Sokolov also discloses tht the ratio of the fluorescence intensity observed from molecules near a roughened silver surface to that from molecules adsorbed on a reference glass substrate can be described by the product of two terms,

$$Y = |L(\omega_{exc})|^2 Z(\omega_{flu}).$$

The term $|L(\omega_{exc})|^2$ is the enhancement of the local electromagnetic field intensity near the nanosized metal structures at the excitation frequency ω_{exc}. It is representative of the ability of the metal to concentrate the electromagnetic energy when the excitation wavelength is coincident with the surface plasmon resonance of the metal. The second factor, $Z(\omega_{flu})$, describes the relative radiative yield of the excited dye molecules of the two substances. (Page 3900, Results and Discussion, first paragraph and the first 2 lines of the second paragraph).

2. Arguments

Previously presented, independent claim 46 recites in relevant part,

"wherein one or more metal particles and at least one of said one or more biomolecules in said sample are positioned at a distance apart sufficient to affect electromagnetic radiation emission of at least one of said one or more biomolecules upon exposing said system to exciting electromagnetic radiation".

Sokolov merely discloses that the dye molecule, i.e., fluorescein, , which labels the phospholipid, i.e., a biomolecule, or which is conjugated with biotin, i.e., a biomolecule, may be excited when positioned near a metal film. Sokolov is measuring the fluorescence of the dye molecule, which is associated with either the phospholipid or biotin.

Applicant respectfully submits that it is the phospholipid and the biotin, respectively, of Sokolov, which should be analogized to the biomolecule of the present invention. Fluorescein, as is well known to those in the art, is a commonly used fluorescent dye.

The present invention clearly describes one or more metal particles and at least one of the one or more biomolecules … are positioned at a distance apart sufficient to affect electromagnetic radiation emission of at least one of said one or more biomolecules upon exposing said system to exciting electromagnetic radiation. (emphasis added). That is, radiative emission of the biomolecule, of the present invention, is effected by positioning at a distance of the metal particles and the biomolecules. In contrast, Sokolov clearly describes a change in radiative yield of the label (conjugate), i.e., fluorescein, and not a change in the radiative yield of

the biomolecule, i.e., the phospholipid or biotin.

Therefore, Applicant respectfully submits that Sokolov does not disclose, teach or suggest at least the present invention's features of: "wherein one or more metal particles and at least one of said one or more biomolecules in said sample are positioned at a distance apart sufficient to affect electromagnetic radiation emission of at least one of said one or more biomolecules upon exposing said system to exciting electromagnetic radiation", as recited in previously presented, independent claim 46. Accordingly, Sokolov does not anticipate the subject matter of previously presented, independent claim 46, and dependent claims 47, 48, 52-56, 59, and 61-66 under 35 U.S.C. §102(b). Withdrawal of the rejection of claims 46-48, 52-56, 59, and 61-66 under 35 U.S.C. §102(b) over Sokolov is respectfully solicited.

B. The 35 U.S.C. 103(a) Rejection over Vo-Dinh (1998) and Vo-Dinh (2000)

1. The Vo-Dinh (1998) Disclosure

Vo-Dinh (1998) discloses an overview of the development and application of the surface-enhanced Raman scattering (SERS) techniques using metal-coated nanostructures on solid substrates. An introduction to theoretical principles of the SERS effect and the different SERS-active media is presented. The focus is on nanostructured solid substrates and their practical applications in chemical, environmental and biomedical areas. Specific examples of analytical techniques, instruments and sensors developed in the author's laboratory will be discussed to illustrate the usefulness and potential of the SERS techniques. (Abstract).

2. The Vo-Dinh (2000) Disclosure

Vo-Dinh (2000) discloses that optical biosensors can be used for many different types of spectroscopy (e.g., absorption, fluorescence, phosphorescence, Raman, SERS, refraction, dispersion spectrometry, etc.) with different spectrochemical properties recorded. These properties include: amplitude, energy, polarization, decay time and/or phase. Amplitude is the most commonly measured parameter of the electromagnetic spectrum, as it can generally be correlated with the concentration of the analyte of interest. The energy of the electromagnetic radiation measured can often provide information about changes in the local environment

surrounding the analyte, its intramolecular atomic vibrations (i.e., Raman or infrared absorption spectroscopies) or the formation of new energy levels. Measurement of the interaction of a free molecule with a fixed surface can often be investigated based on polarization measurements. ... The decay time of a specific emission signal (i.e., fluorescence or phosphorescence) can also be used to gain information about molecular interactions since these decay times are very dependent upon the excited state of the molecules and the local molecular environment. (Page 545, Section 2.2.1 Optical techniques to page 546, line 9).

3. Arguments

Previously presented, independent claim 28 recites in relevant part,

"wherein said one or more metal particles and at least one of said one or more biomolecules in said test sample are positioned at a distance apart sufficient to affect intrinsic emission of electromagnetic radiation of at least one of said one or more biomolecules upon exposing said system to exciting electromagnetic radiation".

Similarly, previously presented, independent claim 67 recites in relevant part,

"wherein said metal particle and at least one of said one or more biomolecules are positioned at a distance apart sufficient to affect intrinsic emission of electromagnetic radiation of at least one of said one or more biomolecules upon exposing said metal particle to exciting electromagnetic radiation".

Vo-Dinh (1998) merely discloses an overview of surface-enhanced Raman scattering (SERS) techniques using metal-coated nanostructures on solid substrates.

However, as is known to one of ordinary skill in the art, Raman scattering (and also, surface-enhanced Raman scattering) operate by completely different physical laws than those of the fluorescent emission used by the present invention.

When light is scattered from a molecule, most photons are elastically scattered. These scattered photons have the same energy (and frequency) and, therefore, wavelength as the incident photons. However, a small fraction of the incident photons (approximately, 1 in 10^7 photons) are inelastically scattered at frequencies (and energies) different from, and usually

lower than, the frequency of the incident photons. The process leading to this inelastic scattering is called the Raman effect. Typically, the inelastically scattered photons differ in energy from the elastically scattered photons by energy levels corresponding to vibrational, rotational, or electronic energy levels of the molecule. (See, for example, kosi.com/raman/resources/tutorial).

Thus, in the Raman scattering used by Vo-Din (1998) incident photons are inelastically scattered and detected by spectroscopes. That is, the same photons are incident and then inelastically scattered.

In contrast, the present invention uses the physical phenomenon of intrinsic (i.e., located within the biomolecule) emission of electromagnetic radiation, i.e., fluorescence. As is known to those of ordinary skill in the art, fluorescence is a luminescence, in which the molecular absorption of a photon triggers the emission of another photon with a longer wavelength. The energy difference between the absorbed and emitted photons typically ends up as molecular vibrations or heat. Fluorescence occurs when a molecule, atom or nanostructure relaxes to its ground state after being electrically excited (i.e., upon absorption of the incident photon). (See, for example, en.wikipedia.org/wiki/fluorescent).

Thus, in the intrinsic emission of the present invention, one incident photon is absorbed by a, for example, molecule, and another photon, after a delay, is emitted.

Therefore, the inelastically scattered photons of Vo-Dinh (1998) are not intrinsic emissions, which are described by the claims of the present invention. Applicant respectfully asserts that Raman scattering and intrinsic emission operate by entirely different and non-analogous physical laws.

For at least the reasons outlined above, Applicant respectfully submits that Vo-Dinh (1998) does not disclose, teach or suggest at least the present invention's features of: "wherein said one or more metal particles and at least one of said one or more biomolecules in said test sample are positioned at a distance apart sufficient to affect intrinsic emission of electromagnetic radiation of at least one of said one or more biomolecules upon exposing said system to exciting electromagnetic radiation", as recited in previously presented, independent claim 28; and "wherein said metal particle and at least one of said one or more biomolecules are positioned at a distance apart sufficient to affect intrinsic emission of electromagnetic radiation of at least one of

said one or more biomolecules upon exposing said metal particle to exciting electromagnetic radiation", as recited in previously presented, independent claim 67.

Vo-Dinh (2000) merely discloses that optical biosensors can be used for many different types of spectroscopy (e.g., absorption, fluorescence, phosphorescence, Raman, SERS, refraction, dispersion spectrometry, etc.) with different spectrochemical properties recorded. For example, Vo-Dink (2000) discloses that the decay time of a specific emission signal (i.e., fluorescence or phosphorescence) can also be used to gain information about molecular interactions since these decay times are very dependent upon the excited state of the molecules and the local molecular environment.

However, Applicant respectfully submits that Vo-Dinh (2000) does not disclose, teach or suggest at least the present invention's features of: "wherein said one or more metal particles and at least one of said one or more biomolecules in said test sample are positioned at a distance apart sufficient to affect intrinsic emission of electromagnetic radiation of at least one of said one or more biomolecules upon exposing said system to exciting electromagnetic radiation", as recited in previously presented, independent claim 28; and "wherein said metal particle and at least one of said one or more biomolecules are positioned at a distance apart sufficient to affect intrinsic emission of electromagnetic radiation of at least one of said one or more biomolecules upon exposing said metal particle to exciting electromagnetic radiation", as recited in previously presented, independent claim 67.

For at least the reasons outlined above, Applicant respectfully submits that Vo-Dinh (1998) and Vo-Dinh (2000), either individually or in combination, do not disclose, teach or suggest at least the present invention's features of: "wherein said one or more metal particles and at least one of said one or more biomolecules in said test sample are positioned at a distance apart sufficient to affect intrinsic emission of electromagnetic radiation of at least one of said one or more biomolecules upon exposing said system to exciting electromagnetic radiation", as recited in previously presented, independent claim 28; and "wherein said metal particle and at least one of said one or more biomolecules are positioned at a distance apart sufficient to affect intrinsic emission of electromagnetic radiation of at least one of said one or more biomolecules upon exposing said metal particle to exciting electromagnetic radiation", as recited in previously

presented, independent claim 67. Accordingly, Vo-Dinh (1998) and Vo-Dinh (2000), either individually or in combination, fail to render obvious the subject matter of previously presented, independent claims 28 and 67, and dependent claims 30-43, 45, and 70-82 under 35 U.S.C. §103(a). The rejection of claims 28, 30-43, 45, 67, and 70-82 under 35 U.S.C. §103(a) over Vo-Dinh (1998) and Vo-Dinh (2000) is respectfully solicited.

II. Formal Matters and Conclusion

Claims 28, 30-43, 45-56, 59, 61-67, and 70-82 are pending in the application.

With respect to the rejections of the claims over the cited prior art, Applicants respectfully argue that the present claims are distinguishable over the prior art of record. In view of the foregoing, the Examiner is respectfully requested to reconsider and withdraw the rejections to the claims.

In view of the foregoing, Applicants submit that claims 28, 30-43, 45-56, 59, 61-67, and 70-82, all the claims presently pending in the application, are in condition for allowance. The Examiner is respectfully requested to pass the above application to issue at the earliest time possible.

Should the Examiner find the application to be other than in condition for allowance, the Examiner is requested to contact the undersigned at the local telephone number listed below to discuss any other changes deemed necessary.

Please charge any deficiencies and credit any overpayments to Attorney's Deposit Account Number 50-3631.

Respectfully submitted,

Dated: October 30, 2008

/Peter A. Balnave/
Peter A. Balnave, Ph.D.
Registration No. 46,199

Gibb & Rahman, LLC
2568-A Riva Road, Suite 304
Annapolis, MD 21401
Voice: (410) 573-5255
Fax: (301) 261-8825
Email: Balnave@Gibb-Rahman.com
Customer Number: 29154